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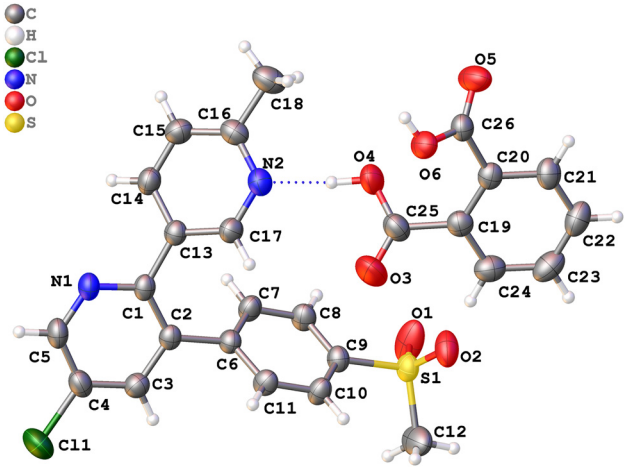
The co-crystal structure of etoricoxib–phthalic acid (1/1), $C_{18}H_{15}ClN_2O_2S{\cdot}C_8H_6O_4$



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Abstract

$C_{18}H_{15}ClN_2O_2S{\cdot}C_8H_6O_4$, triclinic, $P\bar{1}$ (no. 2), a = 8.4340(17) Å, b = 12.172(2) Å, c = 12.816(3) Å, α = 89.98(3)°, β = 77.41(3)°, γ = 72.52(3)°, V = 1221.7(5) Å^3, Z = 2, $R_{gt}(F)$ = 0.0482, $wR_{ref}(F^2)$ = 0.1344, T = 293 K.

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

1 Source of material

In representative experiments, the etoricoxib (ETR) was presented by Nanjing Pujun Technology Co., Ltd. with no further purification. A mixture of ETR (35.9 mg, 0.1 mmol) and phthalic acid (16.6 mg, 0.1 mmol) was dissolved in a mixture of 5.0 mL methanol, and the resulting mixture was stirred and dissolved at 60 °C to obtain a clear solution. Then the solution was filtered and placed in a sample vial, covered with membrane and punctured. Crystals of the title compound were obtained by slow evaporation of the solution at room temperature within one week.

Table 1: Data collection and handling.

Crystal:	Block
Size:	0.30 × 0.20 × 0.10 mm
Wavelength:	Mo *Kα* radiation (0.71073 Å)
μ:	0.29 mm^{-1}
Diffractometer, scan mode:	Nonius CAD4, $\omega/2\theta$
θ_{max}, completeness:	25.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	4813, 4484, 0.022
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3445
$N(param)_{refined}$:	333
Programs:	Olex2 [1], SHELX [2, 3]

1.1 Experimental details

The crystal structure was determined using a CAD4 diffractometer. Using Olex2 [1], the structure was solved with the ShelXT [2] and refined with the ShelXL [3] refinement package. The H atoms were placed in idealized positions and treated as riding on their parent atoms, with the d (C–H) = 0.96 Å (methyl) and d (C–H) = 0.93 Å (aromatic) and d (O–H) = 0.85 Å. And U_{iso}(H) = 1.2 times U_{iso}(C) and U_{iso}(H) = 1.5 times U_{iso}(O).

2 Comment

Etoricoxib (ETR), a selective inhibitor of cyclooxygenase-2, is used to treat osteoarthritis, rheumatoid arthritis, and acute gouty arthritis. According to the biopharmaceutics classification system (BCS) [4], etoricoxib is classified as a BCS class II drug due to its poor aqueous solubility, which limits its clinical application [5, 6]. A cocrystal was reported to improve the physical and chemical stability, dissolution rate, and mechanical properties of drugs [7]. To date, four cocrystals including ETR–succinic acid, ETR–glutaric acid, ETR–adipic acid, ETR–suberic acid and ETR–caprolactam have been reported [8, 9].

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.7979 (3)	0.8052 (2)	0.67913 (19)	0.0327 (5)
C2	0.6951 (3)	0.8191 (2)	0.78274 (19)	0.0331 (5)
C3	0.7117 (3)	0.8959 (2)	0.8556 (2)	0.0393 (6)
H3	0.645914	0.906262	0.925346	0.047*
C4	0.8249 (4)	0.9571 (2)	0.8254 (2)	0.0429 (6)
C5	0.9204 (3)	0.9411 (2)	0.7220 (2)	0.0432 (6)
H5	0.995820	0.983452	0.701181	0.052*
C6	0.5613 (3)	0.7616 (2)	0.81917 (19)	0.0335 (5)
C7	0.4259 (3)	0.7770 (2)	0.7700 (2)	0.0388 (6)
H7	0.423795	0.817002	0.708281	0.047*
C8	0.2943 (3)	0.7332 (2)	0.8123 (2)	0.0397 (6)
H8	0.202502	0.745002	0.779954	0.048*
C9	0.2995 (3)	0.6715 (2)	0.9029 (2)	0.0348 (5)
C10	0.4367 (3)	0.6523 (2)	0.9510 (2)	0.0392 (6)
H10	0.441169	0.609088	1.010778	0.047*
C11	0.5665 (3)	0.6978 (2)	0.9093 (2)	0.0377 (6)
H11	0.658356	0.685877	0.941589	0.045*
C12	0.0775 (4)	0.6434 (3)	1.0905 (3)	0.0680 (10)
H12A	−0.017065	0.616351	1.121524	0.102*
H12B	0.045665	0.725394	1.105693	0.102*
H12C	0.173102	0.605887	1.120582	0.102*
C13	0.7950 (3)	0.7243 (2)	0.59324 (19)	0.0339 (5)
C14	0.8125 (3)	0.7540 (2)	0.4875 (2)	0.0414 (6)
H14	0.825033	0.825437	0.469568	0.050*
C15	0.8110 (4)	0.6772 (2)	0.4101 (2)	0.0464 (7)
H15	0.824773	0.696172	0.339102	0.056*
C16	0.7893 (3)	0.5714 (2)	0.4363 (2)	0.0429 (6)
C17	0.7767 (3)	0.6161 (2)	0.6132 (2)	0.0381 (6)
H17	0.766897	0.593920	0.683164	0.046*
C18	0.7832 (4)	0.4851 (3)	0.3557 (3)	0.0593 (8)
H18A	0.857074	0.410347	0.364826	0.089*
H18B	0.820123	0.507214	0.284777	0.089*
H18C	0.668320	0.482299	0.365528	0.089*
C19	0.5667 (3)	0.2391 (2)	0.7045 (2)	0.0400 (6)
C20	0.5947 (3)	0.1467 (2)	0.6305 (2)	0.0370 (6)
C21	0.4992 (3)	0.0711 (2)	0.6535 (2)	0.0443 (6)
H21	0.513756	0.011761	0.603217	0.053*
C22	0.3827 (4)	0.0829 (3)	0.7505 (3)	0.0527 (7)
H22	0.319539	0.031609	0.765185	0.063*
C23	0.3605 (4)	0.1701 (3)	0.8246 (2)	0.0557 (8)
H23	0.284881	0.176438	0.890730	0.067*
C24	0.4502 (4)	0.2491 (3)	0.8018 (2)	0.0507 (7)
H24	0.432257	0.309217	0.852028	0.061*
C25	0.6434 (4)	0.3351 (2)	0.6823 (2)	0.0480 (7)
C26	0.7259 (3)	0.1241 (2)	0.5279 (2)	0.0386 (6)
Cl1	0.84543 (14)	1.05453 (9)	0.91590 (7)	0.0775 (3)
N1	0.9080 (3)	0.86680 (18)	0.65098 (17)	0.0386 (5)
N2	0.7726 (3)	0.54222 (18)	0.53802 (18)	0.0411 (5)
O1	−0.0081 (3)	0.6699 (2)	0.9084 (2)	0.0741 (7)
O2	0.2015 (3)	0.48969 (17)	0.93349 (18)	0.0595 (6)
O3	0.6801 (4)	0.3835 (3)	0.7501 (2)	0.0923 (9)
O4	0.6550 (3)	0.36536 (18)	0.58412 (17)	0.0552 (6)
H4	0.703 (5)	0.427 (3)	0.571 (3)	0.079 (11)*
O5	0.7049 (3)	0.0924 (2)	0.44496 (16)	0.0648 (6)
O6	0.8711 (2)	0.13690 (17)	0.54007 (15)	0.0468 (5)
H6	0.932151	0.138157	0.481065	0.070*
S1	0.13289 (8)	0.61210 (6)	0.95284 (5)	0.0384 (2)

In the crystal structure, the asymmetric unit contains one ETR molecule and one phthalic acid molecule (see the figure). It indicates that the hydrogen bond plays an important role in maintaining the crystal structure. The N2 atom on the pyridine group of ETR is a hydrogen bond acceptor, and the H atom on the carboxyl (O4–H4) of the phthalic acid molecular is a hydrogen bond donor, forming the intermolecular hydrogen bond O4–H4···N2 [length 1.697 Å, angle 173.1°]. The N2 atom of ETR shows more basic than N1, perhaps because N1 is deactivated as an acceptor by the m-chloro group. The C–C bond lengths of the aromatic rings and bond angles of the phenyl rings were within normal ranges. The C–Cl bond lengths of the benzene ring was 1.730(3) Å. In general, all bond lengths and angles are in the expected ranges in both molecules [10].

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